REMARKS

Upon entry of this Amendment, claims 35-41, 43-47 and 69 are pending herein. By this Amendment, claim 35 is amended, new claim 69 is added and claims 48-68 are canceled. Support for the amendment of claim 35 can be found in the specification, for example, at page 4 lines 30-34. New claim 69 is added to compensate for subject matter deleted from claim 35. Thus, Applicants respectfully submit that this Amendment does not introduce new matter and that the added claim does not introduce new issues.

The attached Appendix includes marked-up copies of each rewritten claim (37 C.F.R. §1.121(c)(1)(ii)).

Entry of the amendments is proper under 37 CFR §1.116 since the amendments: (a) place the application in condition for allowance for the reasons discussed herein; (b) do not raise any new issue requiring further search and/or consideration since the amendments amplify issues previously discussed throughout prosecution; (c) satisfy a requirement of form asserted in the previous Office Action; and (d) place the application in better form for appeal, should an appeal be necessary. The amendments are necessary and were not earlier presented because they are made in response to arguments raised in the final rejection. Entry of the amendments is thus respectfully requested.

I. Drawings

The Office Action requires the submission of corrected drawings. Applicants hereby submit the required corrected formal drawings with a Letter to Official Draftsperson.

II. Restriction/Election

The Office Action withdraws claims 48-68 from consideration. In view of the cancellation of claims 48-68, Applicants submit that the Restriction Requirement is rendered moot and should be withdrawn.

III. Rejection under §112, First Paragraph

Claims 35-41 and 43-47 are rejected under 35 U.S.C. §112, first paragraph, as allegedly non-enabled by the specification. Applicants respectfully traverse this rejection.

As amended, claim 35 specifies that the RNA polymerase is a phage polymerase. Applicants respectfully submit that the scope of the amended claims is fully enabled by the present specification. As admitted by the Office Action, the specification clearly demonstrates the modification of T3 and T7 polymerases to use an RNA template in addition to improved performance of the polymerase using the RNA template.

It is recognized in the art that T3 and T7 polymerases share similar amino acid sequences, chemical activities and physical organization as other RNA polymerases encoded by bacteriophage T7 and its relatives. Furthermore, as described in the specification, from page 4, line 30, to page 5, line 23, the RNA polymerases encoded by bacteriophages such as T7, T3 and SP6 are part of a family of RNA polymerases, generally referred to as the T7-like phages RNA polymerases. The attached Declaration under 37 C.F.R. §1.132 shows that the RNA polymerases encoded by bacteriophage T7, T3 and SP6 were recognized as belonging in the same group and that this group is generally known as the T7-like phage polymerases. Thus, based on the examples provided, the specification provides adequate guidance to enable one skilled in the relevant art to practice the claimed invention.

As indicated in the attached Declaration, it is recognized in the art that the amino acid sequences and overall structure of the region around the active site T7-like phage RNA polymerases, such as T7 RNA polymerase, are highly conserved. The Declaration describes a sequence alignment of different phage RNA polymerases that shows little variation in the amino acid sequences of T7, C21, T3, K11 and SP6 phages between amino acid residues 620 and 640. Because of the highly conserved nature of this region of the RNA polymerase, one

skilled in the art would have expected that a similar mutation in enzymes sharing the same or similar structure would result in the same or similar phenotype.

Based on the examples provided in the specification, it would not have been necessary for one skilled in the art to engage in undue experimentation in order to practice the invention as claimed. Thus, the characterization of the R627A mutant according to the present specification would provide sufficient guidance to enable the use of other T7-like phage RNA polymerases because the amino acid sequences and structures of T7-like phage RNA polymerases are highly conserved in this region (see Attached Declaration).

The number of mutations that one skilled in the art would realistically screen would not be nearly as onerous as suggested by the Office Action. The mutation would be, as discussed above, limited to a conserved area within a T7-like phage RNA polymerase, and success in the outcome of the mutation could be expected and achieved with reasonable certainty.

In addition, the T7-like phage RNA polymerases also recognize a consensus sequence as the promoter. In other words, the T7-like phage RNA polymerases recognize a similar nucleic acid sequence as the transcription start site. The Declaration also describes a comparison of the promoter sequences of several T7-like phage RNA polymerases. The comparison shows that the phage promoters generally share a common 23 bp consensus sequence between nucleotides -17 to +6. Thus, one skilled in the relevant art would understand and appreciate that the claimed phage RNA polymerases also recognize a relatively well-defined consensus sequence within the transcription promoter.

Claim 35 is also amended to delete references to "RNA-dependent" RNA polymerase. As such, Applicants submit that this basis for the rejection is rendered moot.

Again, Applicants submit that the scope of amended claim 35 is fully enabled by the current specification. As amended, the claims do not embrace all RNA polymerases.

Instead, the claims are focused on T7-like phage RNA polymerases, which are recognized in the art as related due to the shared conserved region around the active site of the polymerase as well as the consensus sequence of the promoter that is recognized by the RNA polymerase.

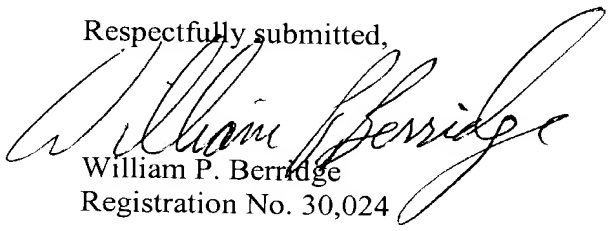
In view of the amendment of claim 35, the above remarks and attached Declaration under 37 C.F.R. §1.132, this rejection should be withdrawn. Reconsideration and withdrawal of the rejection are respectfully requested.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants submit that this application is in condition for allowance. Favorable reconsideration and prompt allowance of the pending claims are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number set forth below.

Respectfully submitted,



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WPB:SXT/amw

Attachments:
Declaration Under Rule 37 C.F.R. §1.132
Appendix

Date: January 16, 2003

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DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461

APPENDIX

Changes to Claims:

Claim 69 is added.

The following is a marked-up version of the amended claim(s):

35. (Twice Amended) A method of amplifying an RNA target sequence, by transcription under the control of a promoter, in an RNA sample comprising said target sequence, said method comprising bringing said sample into contact:

- with a reagent capable of hybridizing with RNA comprising said target sequence,
- in the absence of deoxyribonucleoside triphosphates,
- and with an enzymatic system comprising an ~~RNA-dependent~~ RNA polymerase,

under conditions allowing the hybridization of said reagent with said RNA comprising said target sequence and under conditions allowing the functioning of said ~~RNA-dependent~~ RNA polymerase;

wherein said reagent contains:

(i) a first nucleotide strand comprising: a) a first nucleotide segment capable of playing the role of sense strand of a promoter for said RNA polymerase and b) downstream of said first segment, a second nucleotide segment comprising a sequence capable of hybridizing with a region of said RNA, and

(ii) in the hybridized state on the first strand, a second nucleotide strand comprising a third nucleotide segment capable of hybridizing with said first segment so as to form with it a functional double-stranded promoter;

wherein said RNA polymerase (1) is ~~from a family of~~a T7-like phage RNA polymerases ~~whose promoters have a consensus sequence from position -17 to position -1~~ and (2) is capable of transcribing an RNA template, in the presence of said reagent hybridized with said template, in the absence of associated protein factor and in the absence of a ligase activity.